

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Rajagopalan et al.  
Serial No.: 09/898,887  
Filed: July 31, 2001  
Group Art Unit: 1653  
Confirmation No: 2188  
Examiner: Lukton  
Title: **AROMATIC SULFENATES FOR TYPE I PHOTOTHERAPY**  
Our Ref. No.: MRD-61

Cincinnati, Ohio 45202

February 23, 2005

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**DECLARATION OF RAGHAVAN RAJAGOPALAN**  
**PURSUANT TO 37 C.F.R. §1.132**

Sir:

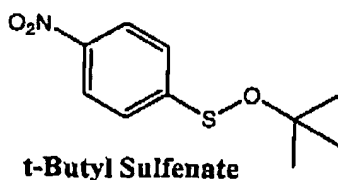
I, RAGHAVAN RAJAGOPALAN, declare as follows:

1. I am a named inventor in the above-identified patent application.
2. I hold a Ph.D. in Organic Chemistry from Columbia University. I have 21 years of experience in the synthesis and use of compounds for medical diagnosis and therapy, which is the subject of the application. I have read the outstanding Office Action of August 25, 2004, and understand the position of the Examiner.

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3. I respectfully assert that the claimed sulfenates are enabled as photosensitizing compounds at least for the following reasons.

4. *para*-nitrophenyl-*tert*-butyl sulfenate, shown by the following structure,



is one example of the claimed core sulfenate compounds, where each of R<sup>1</sup> and R<sup>2</sup> = H, and each of R<sup>3</sup> and R<sup>4</sup> = CH<sub>3</sub>; Ar = benzyl radical; Q = single bond (no targeting moiety attached).

5. Photosensitization of the above sulfenate on cultured cells was evaluated. Specifically, 10  $\mu$ M *para*-nitrophenyl-*tert*-butyl sulfenate was added to flasks containing Lewis lung carcinoma cells ( $2.1\text{--}3.5 \times 10^6$  cells/ml) in phosphate buffered saline in the presence and absence of light (wavelength of about 350 nm) exposure for 30 min and 60 min. Negative controls received no sulfenate and/or no exposure to light. Cell viability was assessed by trypan blue dye exclusion. The following results were obtained.

6. Viability of negative control cells receiving no sulfenate and no light was 86%. Viability of negative control cells receiving no sulfenate, in the presence of either 30 min or 60 min light exposure, was 87% and 82%, respectively.

7. Viability of cells treated for 10 min with sulfenate but with no light exposure was 76%. In contrast, viability of cells treated with sulfenate for 10 min along with light exposure (30 min) was 62.5%, indicating light-induced decreased viability, that is, photosensitivity.

8. Viability of cells treated for 30 min with sulfenate but with no light exposure was 80%. In contrast, viability cells treated with sulfenate for 30 min along with light exposure (60 min) was 66%, again indicating light-induced decreased viability, that is, photosensitivity.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the subject application or any patent issued thereon.

February 24, 2005

Date

Raghavan Rajagopalan

Raghavan Rajagopalan, Ph.D.